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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/730,265	12/09/2003	Daniel Delorme	A1570 CNT2	3328

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EXAMINER	
DESAI, RITA J	
ART UNIT	**PAPER NUMBER**
1625	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/730,265	DELORME ET AL.	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6,15,17,19 and 27-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,15,17,19 and 29-34* is/are rejected.

7)☒ Claim(s) *4,27,28,35 and 36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1,2, 4, 6, 15, 17 and 19 were pending.

Applicants have added new claims 27- 36.

Claims pending 1,2, 4, 6, 15, 17, 19, 27-36

The rejection of claims 1, 2, ,6,15,17, 19 , 29-34 (new claims are also included now) under 35 USC 112 first para still stands.

The rejection is being repeated here.

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
Claims 1, 2, 4, 6, 15, 17 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for R's to a H, does not reasonably provide enablement for all the various substitutions and optionally substituted groups. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.
In re Wands, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).
There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.
1) **The breadth of the claims**: The instant claims encompass many compounds from an aromatic carbocyclic moiety to an aromatic carbocyclic moiety having many large electron withdrawing and bulky groups substituted on it to a moiety having many heterocyclic rings. These compounds cover a very wide range of compounds. It is unclear from the claims what is encompassed.
2) **The nature of the invention**: The invention is a compound for pharmaceutical use.
3) **The state of the prior art:** The state of the art is that pharmaceutical art is highly

unpredictable. The compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group.
The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face..
4) The level of one of ordinary skill: The ordinary artisan is highly skilled.
5) **The level of predictability in the art**: It is noted again that since the pharmaceutical art is highly unpredictable, it requires each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable the area is, the more specific enablement is necessary in order to satisfy the statue.
6) **The amount of direction provided by the inventor:** The inventor provides very little direction in the instant specification. There are few examples and they do not cover the scope of the substitutions and their optionally substituted groups.
7) **The existence of working examples**: The instant specification does not have example commensurate with the scope of the claimed invention. The more unpredictable the art the more examples are required.
8) **The quantity of experimentation** needed to make or use the invention based on the content of the disclosure: Since there are no working examples, the amount of experimentation is very high and burdensome.
Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

Claims employing generic language at the point of novelty, such as applicants', neither provide those elements required to practice the inventions, nor "inform the public" during the life of the patent of the limits of the monopoly asserted. The expression could encompass myriad of compounds and applicants claimed expression represents only an invitation to experiment regarding possible compounds.
In re Kirk, 153 USPQ 48." If you the "public" find that it works, I claim it." is not a proper basis of patentability.

- Applicants argue that the breadth of the claim is as described , which is not correct.

The claims 1 and 2 has a lot more substitutions than as argued.
Claim 1 has a laundry list for R1 and also the Q with its generic describtion includes a plethora of compounds.

R1 is ~~selected from~~ hydrogen,;, a branched or straight Cl-C6 alkyl~;. Cl-C6 alkenyl~ C3-C8 cycloalkylT;_C4-C8(alkyl-cycloalkyl),, wherein alkyl is C1-C2 alkyl and cycloalkyl is C3-C6 cycloalkyl; C6-C~0 aryl. or heteroaryl having from 5 to 10 atoms selected from aay-ef C, S, N and/o._E O.~ wherein t-he said aryl and/o._E heteroaryl may optionally and independently be substituted by 1 or 2 substituents ~~independently~~ selected from eay-elE hydrogen, CH3, (CH2)pCF3, halogen, CONR5R4, COOR5, COR5, (CH2)pN R5R4, (CH2)pCH3,---(CH2)pSOR5R-4, (CH2)pSO2R5, (CH2)pSO2NR5R4 and (CH2)pOR5, wherein p is 0, 1 or 2;

(C1-C2 alkyl)-(C6-Clo aryl), or (C1-C2 alkyl)heteroaryl, t-hewherein said heteroaryl ~~moieties having~~ has from 5 to 10 atoms selected from aa-y-ef C, S, N and/o._E O, and wherein t-he said aryl and/or heteroaryl may optionally and independently be substituted by 1 or 2 substituents .... And so on...

The nature of the invention is of pharmaceutical use and even at the time the invention was made it was clear that the art is unpredictable and very specific.
The state of the prior art: The state of the prior art is that the drugs and the enzymes react in a lock and key mechanism and the structure of the compound has to be specific. Even a difference of a methyl group verses a hydrogen changes the properties altogether. A good example is a theophylline verses caffeine . They differ by just a methyl group but one of them has a pharmaceutical use as a bronchodilator. There is no absolute predictability and no established correlation between the different substitutions on a core that they would all behave in the exact same way. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

- Applicants further argue that the scheme 7 on page 80 and 81 describes how to make theses compounds especially example 55, 56 and 57.

It should be noted that these examples have Q to be a morpholine, piperidine and pyrrolidine and R1 is a H! Thus R1 and Z1 and Z2 are all H.
Thus the teaching of making the compounds does not enable the whole scope.
Applicants haven't even shown what starting material should be used for other compounds.

The availability of the starting material that is needed to prepare the invention as claimed as per MPEP:
A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court in In re Ghiron, 442 F.2d 985, 991,169 USPQ 723, 727 (CCPA 1971), made clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. **The same can be said if certain chemicals are required to make a compound or practice a chemical process.** In re Howarth, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981).

Ex parte Schwarze 151 USPQ 426 (where starting material is not known to art as of date of filing application, there must be included a description of preparation thereof to enable one skilled in this art to carry out applicant's invention), *Ex parte Moersch* 104 USPQ 122 (claims to process for the production of (1)-y1-p-nitrophenyl-2-dichloracetamindo-propane-1,3-diol not enabled because of failure to describe source or method of obtaining starting compound; although starting compound is identified by means of appropriate name and by structural formula).

- Applicants further argue that the other examples 1-53 and 58 onwards have many other substitutions , enough to cover the scope of the claimed invention is incorrect.

None of the examples have and Z1 or Z2, R2 or R3 to be other than hydrogen. Only few limited R1 are shown. This in no way is commensurate with the scope of the claimed invention.

The claims are further drawn to "prodrugs" which are not shown hence the meets and bounds is also not enabled with respect to that.

Pharmaceutical art is highly unpredictable. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), *Ex parte Sudilovsky* 21 USPQ2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain).

Thus in view of the above it would certainly require a considerable amount of undue experimentation to obtain the compounds of the invention.

Hence the rejection still stands.

Claims Objection.

Claim1 is objected to because of the following informalities: The formula for A has a >N=O instead of >C=O . Appropriate correction is required.

Also for R1 C1-C6 alkyl or C4-C8 (alkyl-cycloalkyl) is further defined as wherein alkyl is C1-C2 alkyl. Clarification/correction is required.

Also see the numbering of the claims . There are 2 claims 31.

New Matter rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The applicants have come in and amended the definition of R1 . In particular changes (CH2)pCH3(CH2)pSOR5R4 to read (CH2)pCH3, -(CH2)pSOR5.

This in particular is new matter as it was not described as such in the specifications previously.

Now it reads on the substituent to be a alkyl chain which was not disclosed before.

Conclusion

Claims 1, 2, ,6, 15,17, 19 , 29-34 are rejected.

Claim 4, 27, 28, 35 and 36 are objected to as being dependent from rejected claim.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rita J. Desai
Primary Examiner
Art Unit 1625

R.D
April 11, 2007